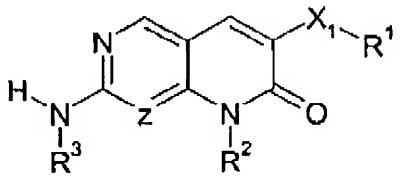
PATENT

WHAT IS CLAIMED:

1. (Original) A compound of Formula I:



Formula I

or a pharmaceutically acceptable salt, hydrate or prodrug thereof,

wherein:

Z is N or CH;

X^1 is O, NR^4 (where R^4 is hydrogen or alkyl), S or C=O;

R^1 is alkyl, cycloalkyl, cycloalkylalkyl or CH_2-alkenyl;

R^2 is hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, haloalkyl, heteroalkyl, cyanoalkyl, alkylene–C(O)–R^{21} (where R^{21} is hydrogen, alkyl, hydroxy, alkoxy, amino, monoalkylamino or dialkylamino), amino, monoalkylamino, dialkylamino, acyl, or NR^{22}-Y-R^{23} (where Y is –C(O), -C(O)O-, -C(O)NR^{24}, $S(O)_2$ or $S(O)_2NR^{25}$; R^{22}, R^{24} and R^{25} are independently hydrogen or alkyl; and R^{23} is hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, heteroalkyl or optionally-substituted phenyl); and

R^3 is alkyl, haloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, cycloalkylalkyl, heteroalkylsubstituted cycloalkyl, heterosubstituted cycloalkyl, heteroalkyl, cyanoalkyl, heterocyclyl, heterocyclylalkyl, or -heterocycloamino-SO_2-R^{12} (where R^{12} is haloalkyl, aryl, aryalkyl, heteroaryl or heteroaralkyl).

2. (Original) The compound of Claim 1, or a pharmaceutically-acceptable salt thereof, wherein X^1 is --O--.

3. (Original) The compound of Claim 2, or a pharmaceutically-acceptable salt thereof, wherein R^1 is alkyl or cycloalkyl.

4. (Original) The compound of Claim 3, or a pharmaceutically-acceptable salt thereof, wherein R^3 is cycloalkyl, cycloalkylalkyl, heteroalkylsubstituted cycloalkyl, heterosubstituted cycloalkyl, heteroalkyl, heterocyclyl or heterocyclylalkyl.

5. (Original) The compound of Claim 4, or a pharmaceutically-acceptable salt thereof, wherein R^3 is cycloalkyl, heteroalkylsubstituted cycloalkyl, heterosubstituted cycloalkyl, heteroalkyl or heterocyclyl.

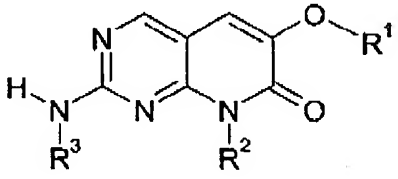
6. (Original) The compound of Claim 5, or a pharmaceutically-acceptable salt thereof, wherein R^3 is optionally-substituted heterocyclyl.

7. (Original) The compound of Claim 5, or a pharmaceutically-acceptable salt thereof, wherein R^3 is hydroxyalkyl or alkoxyalkyl.

8. (Original) The compound of Claim 1, or a pharmaceutically-acceptable salt thereof, wherein R^2 is hydrogen, alkyl, aryl, cycloalkyl or heteroalkyl.

9. (Original) The compound of Claim 8, or a pharmaceutically-acceptable salt thereof, wherein R^2 is alkyl or hydroxyalkyl.

10. (Original) A compound according to Claim 1, having the Formula (I''),



(I'')

wherein,

R^1 is alkyl;

R^2 is selected from hydrogen, alkyl, aryl, cycloalkyl and heteroalkyl; and

R^3 is heteroalkyl or heterocyclyl, or a pharmaceutically-acceptable salt thereof.

11. (Original) The compound of Claim 10, or a pharmaceutically-acceptable salt thereof, wherein R^3 is selected from (1-hydroxy-2-methyl)-prop-2-yl, 1-hydroxy-pentan-2-yl, *(S)*-2-hydroxy-1,2-dimethyl-propyl, *(R)*-2-hydroxy-1,2-dimethyl-propyl, (*S*)-2-hydroxy-1-methyl-ethyl, 1-hydroxymethyl-cyclopentan-1-yl, 2-hydroxy-2-methyl-propyl, 3-methoxy-1(2-methoxy-ethyl)propyl, tetrahydro-2H-pyran-4-yl, 1-(methylsulfonyl)piperidin-4-yl, 1-carboxyethyl)piperidin-4-yl, 1,1-dioxidotetrahydro-2H-thiopyran-4-yl, and morpholinyl.

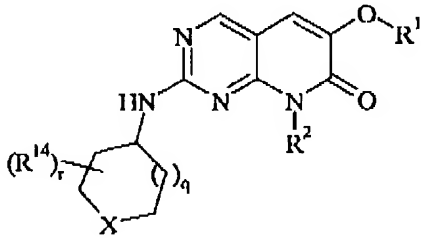
12. (Original) The compound of Claim 10, or a pharmaceutically-acceptable salt thereof, wherein:

R^1 is ethyl;

R^2 is methyl; and

R^3 is selected from (1-hydroxy-2-methyl)-prop-2-yl, 1-hydroxy-pentan-2-yl, *(S)*-2-hydroxy-1,2-dimethyl-propyl, *(R)*-2-hydroxy-1,2-dimethyl-propyl, (*S*)-2-hydroxy-1-methyl-ethyl, 1-hydroxymethyl-cyclopentan-1-yl, 2-hydroxy-2-methyl-propyl, 3-methoxy-1(2-methoxy-ethyl)propyl, tetrahydro-2H-pyran-4-yl, 1-(methylsulfonyl)piperidin-4-yl, 1-carboxyethyl)piperidin-4-yl, 1,1-dioxidotetrahydro-2H-thiopyran-4-yl, and morpholinyl.

13. (Original) The compound of Claim 10, or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, having the formula:



wherein:

X is –O–, –C(=O)–, –N(R^{12a})–, or –CH(R^{12b})–;

R^{12a} is selected from hydrogen, C_{1-4}alkyl, –C(=O)R^{15}, –C(O)$_2R^{15}$, and - S(O)$_2$(C_{1-4}alkyl);

R^{12b} is selected from hydrogen, C_{1-4}alkyl, $-OR^{15}$, $-C(=O)R^{15}$, $-C(O)_2R^{15}$, and $-S(O)_2(C_{1-4}$alkyl); R^{14} is selected from C_{1-4}alkyl, oxo (=O), $\cdot OR^{15}$, $-C(=O)R^{15}$, $-C(O)_2R^{15}$, and $-S(O)_2(C_{1-4}$alkyl); and R^{15} is at each occurrence independently selected from each other R^{15} from hydrogen and C_{1-4}alkyl;
q is 0 or 1; and
r is 0, 1 or 2.

14. (Original) The compound of claim 13, or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, wherein X is $-N(R^{12a})-$, and R^{12a} is $-S(O)_2(C_{1-4}$alkyl).

15. (Original) A pharmaceutical composition comprising:
a pharmaceutically acceptable excipient; and a compound of Claim 1 or a pharmaceutically acceptable salt thereof.

16. (Original) A method for treating a p38 mediated disorder comprising administering to a patient in need of such treatment, an effective amount of a compound of Claim 1.

17. (Original) The method of Claim 16, wherein said p38 mediated disorder is rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, Crohns disease, irritable bowel syndrome, inflammatory bowel disease, psoriasis, adult respiratory distress syndrome, asthma, or chronic obstructive pulmonary disease.

18. (Original) The method of Claim 16, wherein said p38 mediated disorder is Alzheimer's disease.